Titel

Cochlear activity in silent cue-target intervals shows a theta rhythmic pattern and is correlated to attentional alpha modulations

Authors

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Abstract

There is still a controversial debate regarding, where in the processing hierarchy of the central nervous system (CNS) selective attention takes effect. The auditory system can influence cochlear processes via direct and mediated (by the inferior colliculus) projections from the auditory cortex to the superior olivary complex (SOC). Studies illustrating attentional modulations of cochlear responses have so far been limited to sound evoked responses. The aim of the present study was to investigate intermodal (audiovisual) selective attention in humans simultaneously at the cortical and cochlear level during a stimulus-free cue-target period. We found that cochlear activity in the silent cue-target periods was modulated by a theta-rhythmic pattern (~4 Hz). While this pattern was present independently of attentional focus, cochlear theta activity was clearly enhanced when attending to the upcoming auditory input. On a cortical level classical posterior alpha and beta power enhancements were found during auditory selective attention. Interestingly, participants with a stronger attentional modulation of cochlear theta activity show to lesser extent the classical posterior alpha effect. These results hint at a putative theta-rhythmic sampling of auditory input at the cochlear level. Furthermore, our results point to an interindividual variability to what extent efferent pathways are engaged in an attentional context and linked to neural processes outside of the auditory system.

Introduction

Cognitive processing of sensory stimuli is capacity limited. Hence, attentional processes are required to prioritize cognitive resources on task- or context-relevant stimuli. On a neural level, responses to the attended stimulus are enhanced, while responses to unattended and distracting stimuli are diminished (Couperus & Mangun, 2010; Fritz, Elhilali, David, & Shamma, 2007). These effects have been mainly established on a cortical level (Julia Natascha Frey, Ruhnau, & Weisz, 2015; Shrem & Deouell, 2017), however to what extent selective attention modulates subcortical activity is less clear (Guinan, 2018). For the auditory system, this dispute extends down to the level of the cochlea (Giard, Collet, Bouchet, & Pernier, 1994; Hernandez-Peon, Scherrer, & Jouvet, 1956; Meric & Collet, 1994; Picton, Hillyard, Galambos, & Schiff, 1971). Indeed cochlear processes can be influenced via direct and mediated (by the inferior colliculus) projections from the auditory cortex to the superior olivary complex (SOC). The SOC finally innervates the outer hair cells (OHC) that are essential for cochlear amplification and fine tuning of the basilar membrane (Paul H. Delano & Elgoyhen, 2016). The architecture of the efferent auditory system would thus in principle enable such attentional modulations (Terreros & Delano, 2015). This notion is supported by increasing number of studies suggest measuring by otoacoustic emissions (OAE; Smith, Aouad, & Keil, 2012; Walsh, Pasanen, & McFadden, 2015; Wittekindt, Kaiser, & Abel, 2014) or cochlear microphonics (Delano, Elgueda, Hamame, & Robles, 2007) during selective attention tasks. However, the described effects have been restricted to sound evoked responses and have been small and sometimes contradictory (Francis et al., 2018; Meric & Collet, 1992). Furthermore, the attention research focusing on cortical and cochlear processes has been largely conducted independently (see Wittekindt et al. (2014) & Dragicevic et al. (2019) for an exception). In summary, whether and how attention modulates cochlear activity during silent periods and to what extent these peripheral processes are linked to cortical modulations remain unclear.

To advance these issues, we applied an established intermodal (audiovisual) selective attention task and measured activity from different levels of the auditory system simultaneously. To stay as close as possible to previous M/EEG works in this domain (Foxe, Simpson, & Ahlfors, 1998; Julia N. Frey et al., 2014), we decided to record sounds within the ear canal during the silent cue-target period. Since undesired sound-evoked cochlear changes are circumvented, this “ongoing otoacoustic activity” (OOA) allows an unbiased measurements of cochlear modulations by cortical attention processes (Guinan, Backus, Lilaonitkul, & Aharonson, 2003). Given that attentional modulations of cortical oscillations

are most strongly found in at low frequencies (<30 Hz), a novel approach to analyze the OOA-signal was utilized allowing to investigate oscillatory cochlear activity in a similar frequency range. Furthermore, genuine periodic components (peaks) of the OOA-signal (Haller et al., 2018) were computed for the OAA. Replicating an established finding from several previous studies (Fu et al., 2001; Klimesch, 2012; Wittekindt et al., 2014), we show strong attentional modulation of visual cortical alpha activity. More importantly, we illustrate for the first time a rhythmic modulation of cochlear activity in the theta frequency range. While this theta activity was generally present independent of attentional focus, it was strongly amplified when attending to the auditory modality. Interestingly, this attentional amplification of cochlear activity is furthermore inversely correlated with the attentional alpha effects at the cortical level across participants.

Methods

Participants

25 healthy volunteers (16 females, age range: 18-35 years) participated in this study. One participant was completely excluded from analyses because his right ear was occluded by cerumen. As recording otoacoustic activity inside a MEG system is challenging, several participants were furthermore excluded from the final analysis (see below in the results section for details). One participant was excluded because the left acoustic meatus was too small to fit the foam ear tip without causing pain. One participant was excluded because the recordings from the left ear showed excessive periods of saturation. Another four participants were excluded because the number of artifact contaminated MEG trials exceeded 2 standard deviations of the mean. The remaining 18 volunteers (12 female, mean age: 22.17 years, age range: 18-35 years) were used for analyses. One participant was left handed and one was ambidextrous. None of the participants reported any known hearing deficit and any visual impairment was sufficiently corrected. Beforehand, all subjects were informed about the experimental procedure and the purpose of the study and gave written informed consent. As compensation subjects received either 10 Euro per hour or credit for their psychology studies. This study was approved by the Ethics Committee of the University of Salzburg.

Stimuli and Procedure

The focus of this study was the investigation of intermodal selective attention by simultaneously measuring cochlear (OOA) and neuronal processes (MEG). Studies

investigating attentional modulations of OAEs in the past often used a block design (Froehlich, Collet, Valatx, & Morgon, 1993; J. L. Puel, Bonfils, & Pujol, 1988; Smith et al., 2012). As this procedure is getting criticized for not achieving highly controlled attentional conditions (Carrasco, Ling, & Read, 2004; Ward, 1997; Wittekindt et al., 2014), we decided to use an adapted version of the trial-wise cueing paradigm introduced by Wittekindt et al. (2014).

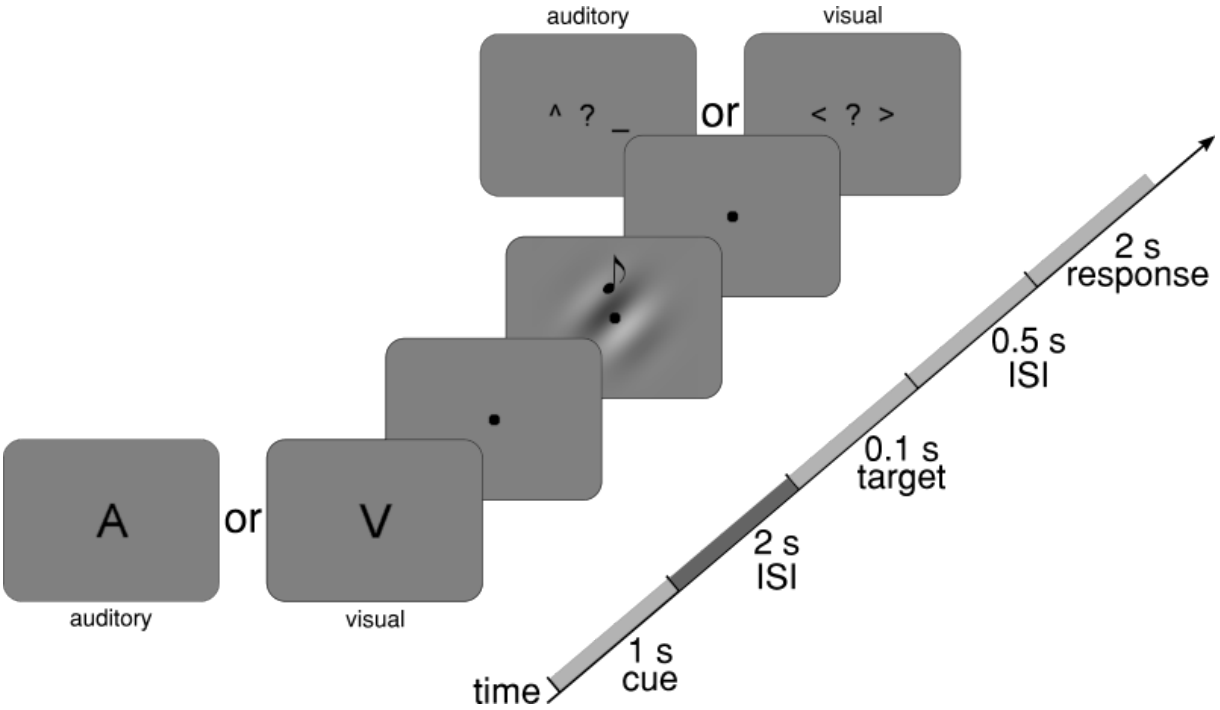

Figure 1. Schematic illustration of the task. Each trial started with a 100% informative visual cue telling the subject to either attend the auditory ("A") or the visual modality ("V"). After an ISI of 2 s a left or right oriented Gabor patch and a low-frequency (1131 Hz) or high-frequency (1987 Hz) pure tone were simultaneously presented. After another ISI of 0.5 s a response screen depending on the cued modality appeared for 2 s. The intertrial interval was uniformly jittered between 1 – 2 s.

Measurements took place in a magnetically shielded room (AK3B, Vacuumschmelze, Hanau, Germany), in which subjects sat quietly inside the MEG system (TRIUX, MEGIN-Elekta Oy, Helsinki, Finland). Participants performed five blocks consisting of 80 trials (40 Attend Auditory and 40 Attend Visual) in a pseudo-randomized order. **Figure 1** schematically illustrates the course of a trial. Each trial started with a visually presented cue (1 s duration) instructing the subject to either attend the auditory or the visual modality. The letter "A" indicated the Attend Auditory condition and the letter "V" the Attend Visual condition. During the following silent cue-target period (2 s duration) a fixation dot was

presented and the participants had to shift their attention selectively to the indicated modality. To eliminate any effects of divided attention and to reach maximal focusing on the cued modality the cue was 100% informative (Wittekindt et al., 2014). The target stimulus in the visual modality was a low contrast Gabor patch (diameter: ca. 2 degrees of visual angle) that was displayed in the center of a rear projection screen placed inside the shielded room (distance: 1.1 m) and was oriented 45 degrees to the right or left. The target stimulus in the auditory modality was a pure tone of either 1131 Hz or 1987 Hz, which was presented via ear inserts. The sound volume was individually adjusted to be at a comfortable level. Visual and auditory stimuli were simultaneously presented for 100 ms. For the auditory stimuli, we employed two 5 ms linear fade in/out windows. Depending on the preceding cue, the task was to detect the orientation of the Gabor patch (Attend Visual, left or right 45° tilt) or the pitch level of the tone (Attend Auditory, high pitch (1987 Hz) or low pitch (1131 Hz)). Afterwards, a response screen showed indicators for choosing either the pitch level of the tone or the orientation of the Gabor patch. The participants were instructed to wait until the response screen was presented (0.5 s post-target), and then reply as soon as they were ready by pressing the corresponding button with their left or right thumb, within 2 s after the appearance of the response screen. The intertrial intervals were jittered uniformly between 1 and 2 s. Acoustic and visual stimuli were generated by the Psychophysics Toolbox Version 3 (Brainard, 1997; Pelli, 1997) using custom-written MATLAB scripts (Version 9.1; The MathWorks).

Recording of Cochlear and Cortical Activity

In order to measure otoacoustic activity a probe consisting of a sensitive microphone and two loudspeakers (ER-10C microphone/preamplifier system, Etymotic Research, Elk Grove Village, US) was fit into the subject's right and left ear canal with a foam ear tip. Otoacoustic activity was recorded from both ears concurrently. The microphone signal was fed into the EEG amplifier of the MEG system, with an amplitude gain of +55 dB (600x). The sampling rate of the entire MEG and EEG system was set to 10 kHz. The ER-10C received its input via two BNC cables coming from a sound preamplifier (SOUNDPixx, VPixx Technologies, Saint-Bruno, Canada). The SPL for the loudspeakers was balanced to the left and right side by subjective feedback for each participant.

Neuromagnetic brain activity was recorded with 306 channels (TRIUX MEG, see above). Additionally, two bipolar electrodes were mounted above and beneath the left eye , one was mounted on the left side of the left eye and another one on the right side of the right eye to monitor eye blinks and eye movements (H/VEOG). Furthermore, two electrodes

were mounted on the bottom left rib and the right collarbone to record electrocardiography (ECG). A reference electrode was placed on the left trapezius muscle, and the ground one on the right supinator. Before the experiment individual head shapes were acquired for each participant including relevant anatomical landmarks (nasion and preauricular points) and about 300 digitized points on the scalp with a 3D digitizer (Polhemus FASTRAK, Colchester, US). Head positions of the subjects in the helmet were estimated at the beginning of each block injecting a small current into five (HPI, head position indicator) coils. Again, the overall (MEG+EEG) sampling rate was set to 10 kHz, with a hardware high-pass filter of 0.1 Hz, and an anti-alias low-pass filter with the cut frequency set zo 3330 Hz.

Signal Processing

OOA was first preprocessed by high-pass filtering at 500 Hz (6th order Butterworth IIR), extracting epochs of 3 s duration after cue presentation and manually rejecting trials containing periods of signal saturation or atypical high background noise, for example caused by moving, swallowing, or coughing (average number of rejected trials per participant: 53.83; range across participants: 1-163). As the frequencies of the acoustic targets were at 1132 Hz and 1987 Hz and otoacoustic activity is strongest in the range from 1000-2000 Hz (Puria, 2003), we expected amplitude modulations of the OOA in this range. Moreover, the cue-target period was defined as the period in which intermodal attention processes occur (Wittekindt et al., 2014). In a next step trials were split into two conditions ("Attend Auditory" and "Attend Visual"), averaged over 1.95 s of the cue-target period, and bandpass filtered in 10 Hz steps from 1000-2000 Hz (bandpass window +/- 30 Hz). This resulted in 201 bandpass windows for each participant, which represent the binned cochlear frequency response between 1000 and 2000 Hz. In order to be able to further study any relationship between cochlear activity and brain oscillations (see Results section), we extracted the envelope of the cochlear signal for each of the previous bandpass windows via a Hilbert transform, thus obtaining a signal with a frequency range that is routinely used in electrophysiological evaluations of cognitive tasks. Next, power spectral density (PSD) from 1-45 Hz was calculated for each condition and each Hilbert transformed bandpass window (“mtmfft” fieldtrip implementation with a Hann window). Finally, the bandpass windows were concatenated for each condition resulting in a representation of the amplitude modulation from 1-45 Hz at cochlear response frequencies from 1000-2000 Hz.

The MEG signal was first preprocessed by manually rejecting all bad sensors (average number of rejected sensors per participant: 46.33; range across participants:

25-73), high-pass filtering at 1 Hz (6th order Butterworth IIR), extracting epochs of 3 s duration after cue presentation and down-sampling to 1 kHz. The excessive amount of rejected sensors is caused by magnetic artifacts of the microphone probes, which leads to a saturation of most of the temporal sensors. The detected bad trials in the OOA data were used to reject the same trials in the MEG data. In a next step trials were again split into two conditions (Attend Auditory and Attend Visual). For source level analysis a standard anatomical magnetic resonance imaging (MRI) template provided by the Statistical Parametric Mapping toolbox (Version 12; (Friston, Penny, Ashburner, Kiebel, & Nichols, 2006) was morphed to the individual head shape of each participant using non linear transformation. Sensor space trials were projected into source space using linearly constrained minimum variance (LCMV) beamformer filters (Van Veen, van Drongelen, Yuchtman, & Suzuki, 1997). The aligned brain volumes were also used to create single-shell head models and compute the leadfield matrices (Nolte, 2003). For the template grid we chose a resolution of 1 cm in MNI space. PSD in 1 Hz steps in a frequency range of 1-45 Hz averaged over 1.95 s of the cue-target period was calculated for each condition by a FFT (Hann window). The preprocessing of the OOA and MEG data were conducted by using the open-source FieldTrip toolbox for EEG/MEG data (Oostenveld, Fries, Maris, & Schoffelen, 2011) and custom-written MATLAB scripts (Version 9.1; The MathWorks).

Statistical Analysis

As a first analysis step we investigated if rhythmic modulations of cochlear activity are present. The python (Version 3.7.1) toolbox FOOOF (Haller et al., 2018) was used to parameterize the envelope of the OOA power spectra of each subject and condition. FOOOF allows the examination of putative oscillations (peaks) in the frequency domain and characterizes these regarding their specific center frequencies, amplitude, and bandwidth by separating the periodic and aperiodic components of neural power spectra (Haller et al., 2018).

For statistical analyses an attention modulation index (AMI) of both conditions was calculated using following formula: (Attend Auditory – Attend Visual) / (Attend Auditory + Attend Visual) / 2. A two-tailed one sample t-test against 0 for each the left and right ear was calculated for the AMI averaged across the aforementioned range of 1000-2000 Hz and the amplitude modulation. Given the strong slow frequency dominance and clear theta rhythmicity in all participants (see results), statistical analysis of the AMI was conducted for the 1-10 Hz range. Analogues to OOA the AMI for both conditions of the MEG data was calculated. Uncorrected t-tests against 0 on the frequency range from 1-30 Hz were

conducted. Next, Bonferroni corrected (5% level) t-tests against 0 on source space data for the averaged frequency range from 8-12 Hz and 15-17 Hz were performed. In a next step the AMI of the OOA was correlated with the significant AMI MEG effects. The statistical analyses of the OOA and MEG data were conducted by using the open-source FieldTrip toolbox for EEG/MEG data (Oostenveld et al., 2011) and custom written MATLAB scripts (Version 9.1; The MathWorks).

Results

Behavioural Results

Performance was similar for both conditions and in general very high, underlining the compliance of the participants during the experiment. The average hit rates were M = 92.60 % (SD = 8.11 %) for the auditory task and M = 94.17 % (SD = 7.28 %) for the visual task. The hit rates of the two conditions did not differ significantly ($t_{(17)}$ = -1.721, p = 0.104).

Otoacoustic Activity at Theta Rhythm Is Modulated by Intermodal Attention

Typical oscillatory activity of the brain is located in a frequency band of 1-80 Hz, whereas otoacoustic activity is found at much higher frequencies (500-4000 Hz). As the aim of this experiment is to study the effects of cortical top-down modulations on OOA, we implemented a novel approach for analyzing cochlear oscillatory activity. We applied the Hilbert transform to extract the amplitude modulation for frequencies typical of ongoing cortical oscillations. To avoid a higher influence of the lower sound frequencies and to create a representation of the cochlea's frequency response, the otoacoustic signal was bandpass filtered between 1000 and 2000 Hz in 10 Hz steps with a window size of +/- 30 Hz. The PSDs of the 201 bandpass windows were then concatenated to create a representation of the amplitude modulation between 1000 and 2000 Hz of the cochlea's frequency response.

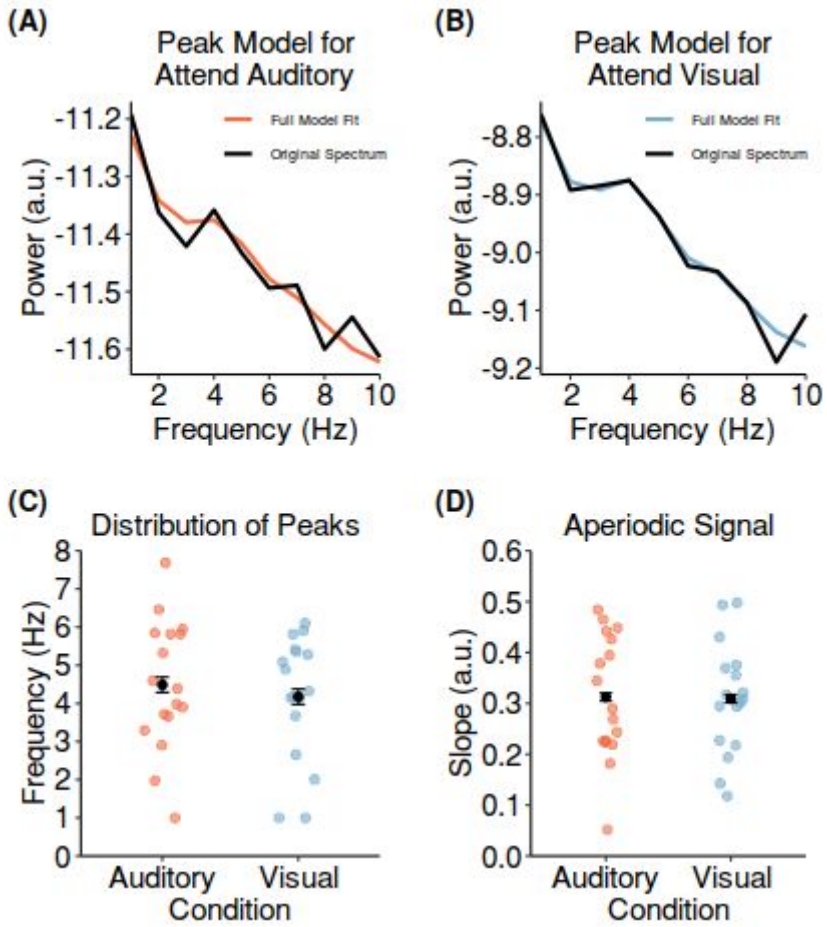

Figure 2. Peak analysis of OOA by FOOOF shows theta rhythmicity of cochlear activity. (A) Example peak model for the Attend Auditory condition (subject 1). The red line demonstrates the full power spectrum fit, which is a combination of the aperiodic fit ("1/f noise") and the number of peaks. (B) Example peak model for the Attend Visual condition (subject 8). The blue line represents the full power spectrum fit, which is a combination of the aperiodic fit ("1/f noise"). (C) Distribution of the lowest peaks for each subject and condition. The black dot and error bars represent the mean and standard error. (D) Distribution of the aperiodic signal for each subject and condition. The black dot and error bars represent the mean and standard error.

In a first step we parameterized oscillatory modulations of OOA during the silent cue-target interval. We used FOOOF to differentiate between genuine oscillatory contributions from aperiodic 1/f changes. **Figures 2A** and **2B** exemplary illustrate the model fits in two subjects for both conditions. In all but one subject a peak could be found at low (< 10 Hz) frequencies: For the Attend Auditory condition the average peak was at 4.35 Hz (*SD* = 1.73) and at 3.98 Hz (*SD* = 1.44) when attending to the visual modality. Which modality was attended to had no statistically significant impact on the peak frequencies ($t_{(16)}$ = 0.9003, p = 0.3813). **Figures 2C** and **2D** show subjects' individual peak frequencies and

model fit for aperiodic components ("1/f noise"). While this analysis overall points to a theta-rhythmic modulation of cochlear activity in a silent cue-target period, the range (1-7.68 Hz) of these peaks points at a rather high interindividual variability.

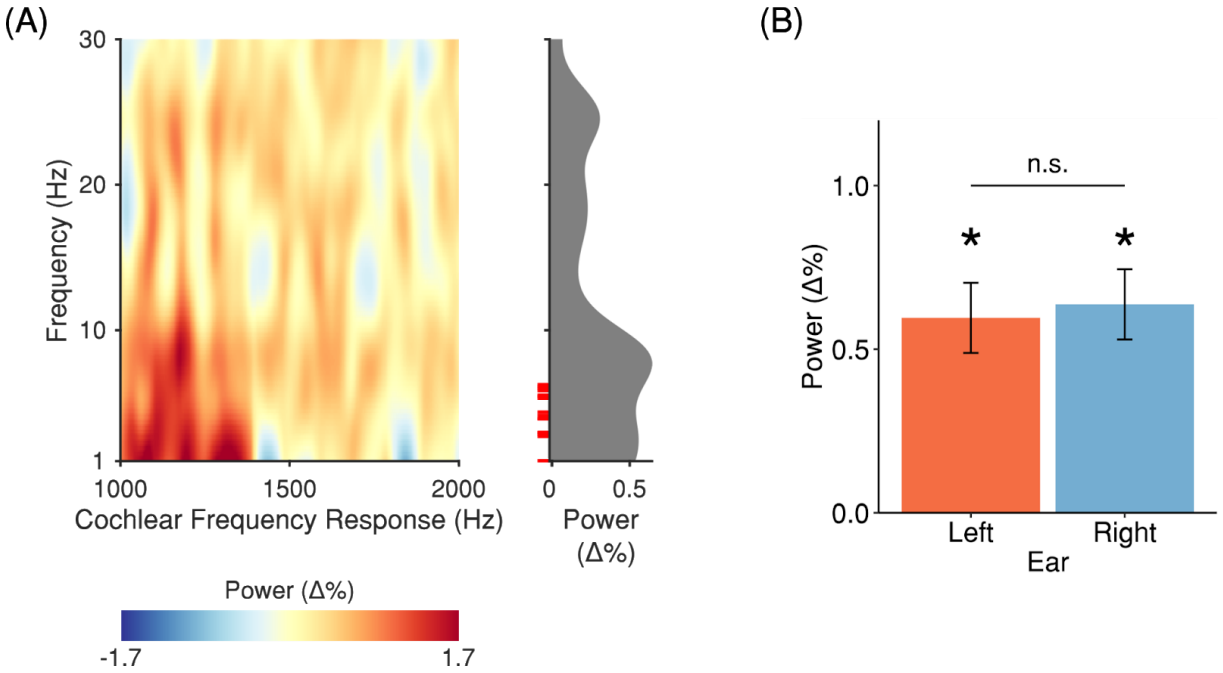

Figure 3. Power analysis of OOA shows enhanced low-frequency power for auditory attention. (A) Contrasted representation of the cochlear frequency response averaged over both ears. The x-axis represents otoacoustic activity at tone frequencies from 1000-2000 Hz. The y-axis represents the frequency range of the FFT. On the right the OOA-AMI averaged from 1000-2000 Hz is shown. The red ticks illustrate the distribution of subjects' peak frequencies from Figure 2C. (B) Contrasted OOA for the left and right ear. The OOA-AMI is significantly higher for the Attend Auditory condition in the left ($t_{(17)}$ = 2.4837, p = 0.0237) and the right ($t_{(17)}$ = 2.6111, p = 0.0183) ear. There was no difference between ears ($t_{(17)}$ = -0.2220, p = 0.8270).

Next, we tested the hypothesis that cochlear activity is elevated during periods of focused auditory attention compared to visual. Descriptively it appears from the grand average that the amplitude (**Figure 3A**) differences of the AMI lie predominantly in the range of low frequencies, corresponding to the frequency range of dominant rhythmic cochlear activity (**Figure 2C**). Given this overlap the AMI was averaged between 1 and 10 Hz for the cochlear response frequency range of 1000-2000 Hz for both ears each. In a next step two-tailed one sample t-tests against zero were performed (see **Figure 3B**). The result for the left ear revealed that cochlear activity (M = 0.0060 %, SE = 0.0024 %) was significantly higher for the Attend Auditory condition ($t_{(17)}$ = 2.4837, p = 0.0237). As for the left ear also

the result of the right ear revealed significantly higher cochlear activity (M = 0.0064 %, SE = 0.0024 %) for the Attend Auditory condition ($t_{(17)}$ = 2.6111, p = 0.0183). No inter-aural differences could be observed ($t_{(17)}$ = -0.2220, p = 0.8270).

Classical Cortical Alpha Power Effects Are Related to Cochlear Changes

In order to assess effects of intermodal attention on brain level, we firstly performed uncorrected t-tests on source projected MEG data over frequencies of 1-30 Hz (see Materials and Methods). The analysis was performed on the AMI of the 1.95 s cue-target interval. The uncorrected t-tests revealed higher power in alpha and low beta bands. Additionally, bonferroni corrected (5% level) t-tests for a frequency range of 8-12 Hz (alpha) and 15-17 Hz (beta) were performed to test these results.

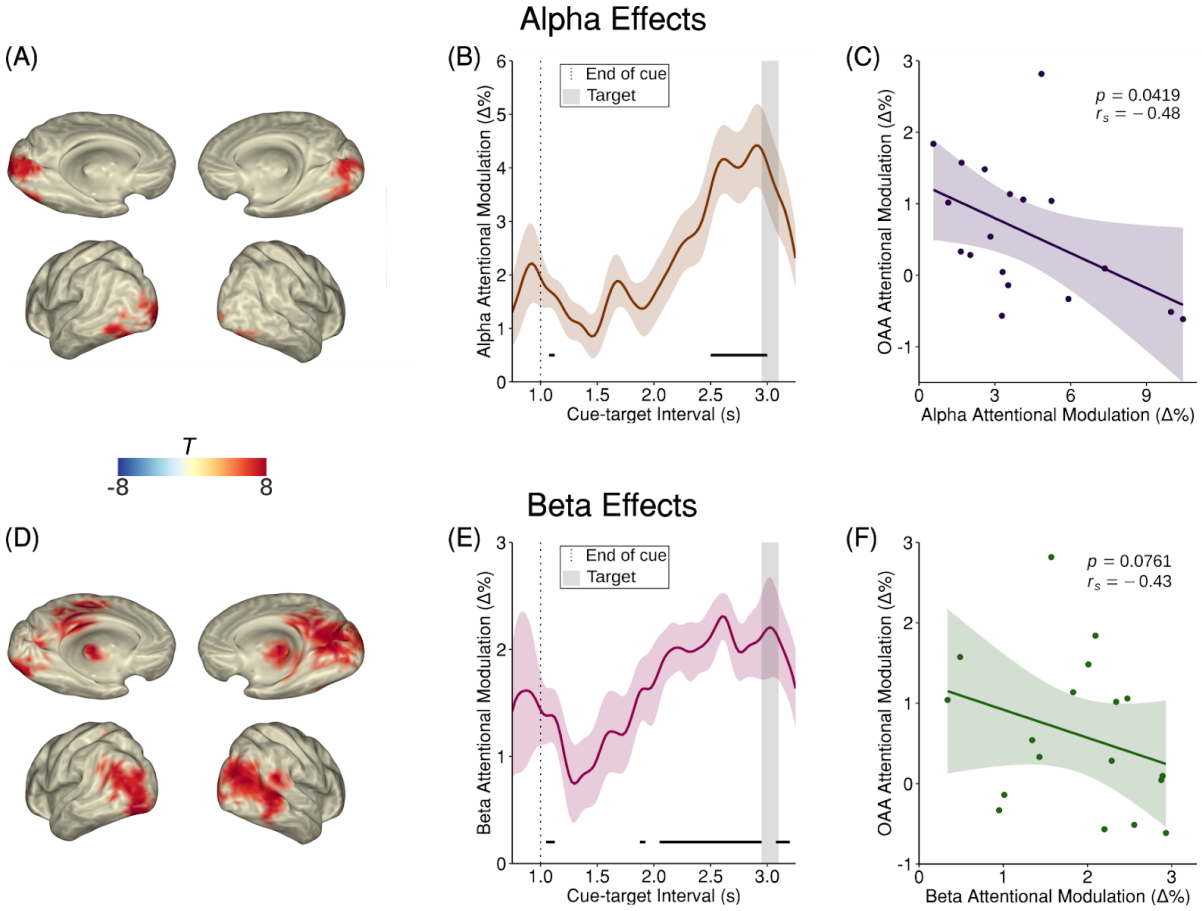

Figure 4. Cortical attention effects and correlation with OOA. (A) Bonferroni corrected statistical contrast alpha-AMI versus 0 of the source reconstruction for the 0-1.95 s cue-target period and 8-12 Hz frequency window. (B) Time course of the alpha-AMI for significant voxels from analysis in (A). The shaded error bar represents the standard error and the bottom black lines the from 0 significantly different time windows on the 5% significance level. (C) Correlation of alpha-AMI (of significant 450 ms interval in (B)) and

OOA-AMI. The shaded error bar represents the standard error. (D) Bonferroni corrected statistical contrast beta-AMI versus 0 of the source reconstruction for the 0-1.95 s cue-target period and 15-17 Hz frequency window. (E) Time course of the beta-AMI for significant voxels from analysis in (A). The shaded error bar represents the standard error and the bottom black lines the from 0 significantly different time windows on the 5% significance level. (F) Correlation of beta-AMI (of significant 1.15 s interval in (E)) and OOA-AMI. The shaded error bar represents the standard error.

We expected an inhibited sensory processing of the currently distracting sensory modality – occipital regions for the visual and temporal regions for the auditory modality. According to dominant frameworks (Klimesch, 2012) this functional inhibition should manifest as increased power in the alpha-band. **Figure 4A** shows significant T-values of a two-tailed t-test against zero of the alpha-AMI. As expected, alpha power is significantly increased for the Attend Auditory condition over the primary visual cortex. However, no increased alpha power for the Attend Visual condition in auditory regions could be found. This absence may be related to a reduced measurement sensitivity due to the significant loss of MEG sensors covering the temporal regions. In order to investigate the temporal dynamics in the cue-target interval, the time course of the alpha-AMI was calculated over the significant voxels in posterior regions (**Figure 4B**). It can be seen that the alpha-AMI starts to increase 1 s after cue presentation. Bonferroni corrected t-tests against zero reveal that the alpha-AMI is significantly increased in a 450 ms interval before target presentation. In order to assess whether this effect found at the cochlear level was associated with the previously described cochlear effects a correlation between the alpha-AMI over the significant 450 ms interval before target presentation and the OOA-AMI was calculated. A significant negative correlation ($r_{s(17)} = -0.4819$, $p = 0.0419$; **Figure 4C**) was found, indicating that individuals engaging efferent processes when attending to auditory input showed less disengagement of visual processing regions. However, in **Figure 4C** it can be noticed that an outlier biases the correlation. A recalculation of the correlation without the outlier resulted in a stronger negative correlation ($r_{s(16)} = -0.6387$, $p = 0.0054$).

Figure 4D shows significantly increased beta power for the Attend Auditory Condition over primary visual cortex and visual association areas. As for the alpha-AMI, the time course of the beta-AMI was calculated over the significant voxels in posterior regions (**Figure 4E**). It can be seen that the beta-AMI starts to increase earlier than the alpha-AMI namely 300 ms after cue presentation. Bonferroni corrected t-tests against zero reveal that the beta-AMI is significantly increased in a 1.15 s interval before target presentation. In the same way as for the alpha-AMI, we calculated a correlation between the beta-AMI over the

significant 1.15 s interval before target presentation and the OOA-AMI. While the generally same negative trend was observed as for alpha, the correlation with beta was not significant ($r_{s(17)}$ = -0.4270, p = 0.0761; **Figure 4F**). Here, the exclusion of the outlier resulted in a hardly stronger negative correlation that was still only significant on a trend level ($r_{s(16)}$ = -0.4328, p = 0.0814).

Discussion

To what extent cochlear activity is sensitive to selective attention and how these changes are linked to cortical dynamics is a matter of ongoing debate. Given the uniqueness of the auditory system in having cortical descending projections from primary auditory cortex (via IC and SOC) to the cochlea, a putative mechanism of alternating attentional states directly affecting the cochlear receptor is conceivable. To pursue our aims we established an entirely new approach for investigating cochlear otoacoustic activity that allows us to draw first conclusions as to how cortical attention processes are linked to cochlear otoacoustic activity. We demonstrate the presence of a theta-rhythmic pattern of otoacoustic activity during silent periods when attention was focused to either upcoming auditory or visual targets. Furthermore, we established a relationship between cochlear theta and cortical alpha modulations during the cue-target periods. Despite several open issues remaining, this study creates a connection between cochlear and cortical attentional modulations and helps closing the distance between the remarkably segregated auditory attention research lines.

Our analysis of the OOA during the cue-target period indicated a genuine rhythmic modulation in the theta frequency range (~4 Hz on average), that was not explicable by aperiodic 1/f contributions to the spectrum. The peak frequency of the found rhythmic OOA pattern is not different between visual and auditory attention, indicating that an endogenous cochlear rhythm at ~4 Hz could exist. At this stage it is unclear whether the observed rhythmicity of the recorded signal is intrinsic to cochlear processes or whether they are a consequence of efferent innervation. To resolve this issue is important also from an active sampling (Schroeder, Wilson, Radman, Scharfman, & Lakatos, 2010) perspective, which points to an omnipresence of theta-like rhythms in various cognitive domains ranging from perception to action (Hasselmo & Stern, 2014; Poeppel, 2003; Spyropoulos, Bosman, & Fries, 2018; Tomassini, Ambrogioni, Medendorp, & Maris, 2017). Extending such views, a recent “rhythmic theory of attention” framework states that attention is theta-rhythmically discontinuous over time (Fiebelkorn & Kastner, 2019; Fries, Reynolds, Rorie, & Desimone,

2001; Landau & Fries, 2012; Wutz, Melcher, & Samaha, 2018). While the latter framework has been developed mainly to better understand visuospatial attention, similar processes may also be relevant in the auditory system. Depending on the generating mechanisms of the 4 Hz cochlear activity, perceptual or attentional rhythmicities could either be genuinely cortically driven effects (with cochlear effects being epiphenomenal) or they (and by extension cortical effects) could be an adaptation to cochlear physiological processes. However, the interindividual difference in peak frequencies was rather high, which hints to different contributions of attention processes on the cochlea.

Beyond the illustration of a slow (theta) rhythmic modulation of OOA during the silent cue-target interval independent of the attention focus, we show that the magnitude of this process is clearly attentionally modulated. We found an enhancement during auditory selective attention, which might reflect an enhancement of cochlear sound amplification. In line with previous studies that found reduced levels of OAEs in subjects attending to a visual task our results resemble an inhibition of the irrelevant and distracting acoustic stimulus during visual selective attention (Froehlich, Collet, Valatx, & Morgon, 1993; Meric & Collet, 1992; Puel, Rebillard, Bonfils, & Pujol, 1989; Wittekindt et al., 2014; see Dragicevic et al. (2019) & Smith et al. (2012) for an exception). Yet, so far all of the studies that investigated effects of attention on the cochlea in humans utilized different types of evoked OAEs (EOAE) and distortion product OAEs (DPOAE). The measurement of EOAEs and DPOAEs needs acoustic elicitor and probe stimuli. Guinan et al. (2003) could demonstrate that this acoustic stimulation is able to alter cochlear properties by itself, which makes them rather unfavorable for assessing pure efferent effects. Here, we utilized OOA that is measured in silent cue-target periods and thus avoids any confounding efferent activity. Moreover, our novel approach allows us to stay as close as possible to previous literature in the cortical attention domain. In the current study we show power modulations of OOA in frequencies that in the cortical literature have been repeatedly reported to be related with various attentional task demands (Fiebelkorn, Pinsk, & Kastner, 2019; Fries et al., 2001; Klimesch, 2012; Wutz et al., 2018). Electrical stimulation of the auditory cortex in bats and chinchillas has shown that cochlear responses can be modulated in a frequency specific manner (Dragicevic et al., 2019; León, Elgueda, Silva, Hamamé, & Delano, 2012; Xiao & Suga, 2002). By this means, these results imply that the modulation of cochlear low-frequency oscillatory power putatively is driven by top-down attentional processes (note that the frequency is unchanged). Given the well established neuroanatomy of the auditory efferent system, corticofugal projections from the auditory cortex to the cochlear receptor, which are mediated by the IC and SOC, are the most probable neural substrates of this effect. This

however remains to be established in future studies, in which technical improvements will allow better sensitivity to auditory cortical processes.

The current results of induced oscillatory activity in the MEG are in accordance with previous results and give an insight into the attentional demands of the task. Despite the unfavourable measurement conditions, we found elevated alpha- and beta-band activity in the pretarget period of Attend Auditory compared with Attend Visual trials in posterior regions but no modulations over auditory regions. Various studies on intermodal selective attention have postulated an active role of cortical alpha oscillations on modulating primary sensory areas (Bauer, Kennett, & Driver, 2012; Foxe et al., 1998; Julia N. Frey et al., 2014; Fu et al., 2001; Wittekindt et al., 2014). In this context alpha-band activity is proposed to reflect a suppression mechanism and especially seems to be relevant if distracting input has to be actively blocked. Two studies employing an audiovisual task have reported alpha power increases in posterior sensors when attention was directed to the auditory modality, power decreases when attention was directed to the visual modality, and no alpha-band modulations over auditory cortices (Foxe et al., 1998; Fu et al., 2001). In line with these findings, Wittekindt et al. (2014) observed a relative posterior alpha power increase when attention was focused on the upcoming auditory compared with the visual target. Our findings that show increased alpha power in primary visual cortex during auditory selective attention are in accordance with this view. In this way, alpha oscillations act to reduce processing of distracting input for the task irrelevant visual modality. The absence of modulations over auditory cortices by alpha-band activity could stem from the reduced sensitivity in temporal regions as most temporal MEG sensors were saturated due to the magnetic artifacts by the microphone probes, but could be caused by the specific demands of this paradigm.

There are only two previous studies that simultaneously recorded DPOAEs and EEG and therefore were able to investigate the relationship between cochlear and brain activity. Wittekindt et al. (2014) failed to show any correlations between those two. The authors explain this by the fact that their found effects depict different mechanisms of selective attention and thus do not depend on each other directly. In contrast, Dragicevic et al. (2019) reported significant correlations between the oscillatory DPOAE signal and cortical oscillations at low frequencies (< 10 Hz) in different periods of the auditory and visual tasks. However, the significance of both studies on attributing their results on top-down attentional modulations is limited by assessing cochlear activity via DPOAEs. As mentioned above, the elicitor stimuli which are required to evoke DPOAEs are prone to elicit MOC efferent activity that causes intrinsic cochlear changes by themselves. Hence, any inferences from

correlations between oscillatory activity of the cochlea and the brain have to be treated with caution. The current study avoids these pitfalls by utilizing OOA in silent periods.

We found evidence for a putative relationship, namely, a negative correlation of cochlear low-frequency (1-10 Hz) power and brain alpha-power during periods of selective attention. It appears that subjects that exhibit stronger inhibition of distracting visual input (by enhanced alpha-power) at the same time, show weaker enhancement of the attended auditory target (by less enhanced low-frequency OAA-power) and vice versa. This inverse relationship could point to the existence of different strategies by the oscillatory attentional network to prioritize attended auditory input in the context of audiovisual attention. In one strategy distracting visual input is effectively prevented from being globally processed. In the other strategy relevant auditory input is enhanced already at the cochlear level, leading to an amplified signal transduction to auditory brain regions. Interindividual variability appears to exist to what extent these alternative strategies are deployed. It would be interesting in future studies to investigate how these processes are manifested in individuals with reported hearing problems with or without audiometric deficits.

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Competing interests

The authors declare no competing interests.

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